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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,518	02/24/2004	John H. Greinwald JR.	CHMC17.001CP1	2735

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EXAMINER	
SALMON, KATHERINE D	

ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
03/26/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/786,518	GREINWALD ET AL.	
	Examiner	Art Unit	
	KATHERINE SALMON	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

1. It is noted that the examiner in application 10/786518 has been changed. Please direct all correspondences to Katherine Salmon, Art Unit 1634.

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/07/2007 has been entered.

3. Claims 17-23 are pending and under consideration. Claims 1-16 and 24 have been cancelled.

Withdrawn Rejections

4. The rejection of the claims made under 35 USC 103(a) made in section 4 of the previous office action is moot based upon arguments made in the reply of 12/07/2007. Specifically that the website was not available before the filing date of 2/24/2003 (p. 4 3rd paragraph of reply).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims17 and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morton et al. (Human Molecular Genetics 2002 Vol. 11 p. 1229) in view of Choo et al. (The Journal of Pediatrics February 2002 p. 148).

With regard to Claim 17, Morton et al. teaches that hundreds of syndromic forms of deafness have been described and the underlying genetic mutation identified for many of the common forms (p. 1231 1st sentence). In Table 1, Morton et al. lists 58 genes associated with hearing loss (claims 7-12). Morton et al. teaches a range of genes for both syndromic or nonsyndromic hearing loss (Table 1). Morton et al. teaches genetic mutations from CDH23, MYO7A, OTOF, SLC26A4, and USH2A (Table 1).

Morton et al., however, does not teach a microarray comprising these genetic mutations.

Morton et al., however, does not teach a screening method to diagnose hearing loss.

Choo et al. teaches that molecular genetics will affect clinical management of pediatric sensorineural hearing loss. With regard to Claims 17, 22-23, Choo et al. teaches that a “deafness gene chip” could be developed to screen newborns for gene mutations that cause or predispose that infant to significant hearing impairment (p. 149 2nd column last sentence and 3rd column 1st paragraph). Choo et al. teaches DNA would be screened on a microarray spotted with cDNAs or oligonucleotides associated with hearing loss (p. 149 3rd column 1st paragraph).

Therefore it would have been prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the list of genes of Morton et al. to attach to a microarray to form a "deaf chip" as taught by Choo et al. to screen for hearing loss with a reasonable expectation of success. The ordinarily artisan would be motivated to place known mutations associated with deafness as taught by Morton et al. onto a microarray as taught by Choo et al. because Choo et al. teaches that microarray technology allows investigators to simultaneously assay the expression of hundreds or thousands of genes (p. 149 2nd column last paragraph). Choo et al. teaches that it is very apparent that a “deafness gene chip” could be developed for purposes of screening newborns for gene mutations that cause or predispose that infant to

significant hearing impairment (p. 149 2nd column last paragraph and 3rd column 1st paragraph). Choo et al. further teaches that "deafness gene chips" allows for more cost-effective, efficient newborn hearing screening with the use of molecular techniques (p. 149 3rd column). Therefore the ordinary artisan would be motivated to place the known gene mutations as taught by Morton et al. onto an array as taught by Choo et al. to screen patients with a large number of gene mutations quickly and efficiently.

7. Claims 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morton et al. (Human Molecular Genetics 2002 Vol. 11 p. 1229) in view of Choo et al. (The Journal of Pediatrics February 2002 p. 148) as applied to claims 17 and 22-23 and in view of Weston et al. (American Journal Human Genetics 1996 Vol 59 p. 1074) and Guo et al., (Guo et at., 2002, Oligonucleotide Arrays for High-Throughput SNPs Detection in the MHC Class I Genes: HLA-B as a Model System, Genome Res., Vol. 12: 447-457)..

The combination of Morton et al. and Choo et al. teach a microarray comprising at least 5 sequences from the group consisting of genetic sequences from CDH23, MYO7A, OTOF, SLC26A4, and USH2A. The combination of Morton et al. and Choo et al. does not teach that the sequences comprise multiple adjacent exon or single exon.

Weston et al. teaches screening of patients with mutations in MYO7A (abstract). With regard to Claims 18-19, Weston et al. teaches detection of mutations of MYO7A within adjacent exon (Exon 13 and 14) (Table 2). With regard to Claims 20-21, Weston

et al. teaches mutations which are present in only one exon (e.g. EXON 3 or 4) (Table 2). Therefore Weston et al. teaches various mutations of MYO7A which are in single exon and are found in a combination of adjacent exon.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention was made to detect any of the mutations of MYO7A in single exon and adjacent exon taught by Weston et al. by a microarray comprising sequences as taught by Morton et al. and Choo et al. with a reasonable expectation of success. The ordinary artisan would be motivated to design sequences on the microarray of Morton et al. and Choo et al. comprising single exon and adjacent exon taught by Weston et al. because Weston et al. teaches that these mutations are associated with hearing loss (abstract). Therefore the ordinary artisan would be motivated to detect on associated the single exon and adjacent exon of MYO7A as taught by Weston et al. to screen patients for genetically associated hearing disorders.

37 CFR 1.132 Declaration

8. The declaration under 37 CFR 1.132 filed 12/07/2007 by John H. Greinwald was presented in view of the 35 USC 103(a) rejection made in the Office Action mailed June 7, 2007. Though this rejection has been withdrawn the 37 CFR 1.132 Declaration has been thoroughly reviewed based on the 35 USC 103(a) rejection of Morton et al. (Human Molecular Genetics 2002 Vol. 11 p. 1229) in view of Choo et al. (The Journal of Pediatrics February 2002 p. 148) presented above. The points made in the 37 CFR 1.132 has been summarized below and responded to.

(A) The 37 CFR 1.132 asserts that current medical evaluation of hearing loss involves a combination of laboratory and radiographic tests (point 7). The 37 CFR 1.132 asserts that beyond the standard GJB2 gene it has been uncertain which gene mutations were most prevalent in patients with hearing loss (point 7). The 37 CFR 1.132 asserts that the array comprising genetic sequence form CDH23, MYO7A, OTOF, SLC26A4, and USH2A addresses a need for a tool for efficient diagnosis of hearing loss (point 7).

This argument has been fully reviewed but has not been found persuasive.

The 37 CFR 1.132 asserts that there has been a long felt need for a tool for efficient diagnosis of hearing loss. The declaration under 37 CFR 1.132 filed 12/07/2008 is insufficient to overcome the rejection of claims 17-23 based upon the 35 USC 103(a) rejections presented above.

Though there is no single piece of art teaching an array comprising CDH23, MYO7A, OTOF, SLC26A4, and USH2A, the combination of Morton et al. and Choo et al. teach that mutations in these genes are associated with hearing loss and motivation to place hearing loss mutations on an array. Therefore the combination of Morton et al. and Choo et al. teach all the limitations of the claims.

The 37 1.132 declaration states that the claimed subject matter solved a problem that was long standing in the art. However, there is no showing that others of ordinary skill in the art were working on the problem and if so, for how long. In addition, there is

no evidence that if persons skilled in the art who were presumably working on the problem knew of the teachings of the above cited references, they would still be unable to solve the problem. See MPEP § 716.04.

(B) The 37 CFR 1.132 asserts that an array comprising genes CDH23, MYO7A, OTOF, SLC26A4, and USH2A would provide an unexpected benefit because detection of the five genes would provide a more comprehensive diagnostic evaluation (point 8). The 37 CFR 1.132 asserts that there was no teaching in the literature to suggest preparing an array comprising CDH23, MYO7A, OTOF, SLC26A4, and USH2A and no reason to expect that such an array would provide a more accurate and cost effective diagnosis of hearing loss in SNHL in children (point 13).

These arguments have been fully reviewed but have not been found persuasive.

The 37 CFR 1.132 has not provided any evidence that the array has an unexpected benefit. Morton et al. teaches all the genes and mutations associated with hearing loss. Choo et al. teaches that microarray technology allows investigators to simultaneously assay the expression of hundreds or thousands of genes (p. 149 2nd column last paragraph). Choo et al. teaches that it is very apparent that a “deafness gene chip” could be developed for purposes of screening newborns for gene mutations that cause or predispose that infant to significant hearing impairment (p. 149 2nd column last paragraph and 3rd column 1st paragraph). Choo et al. further teaches that “deafness

gene chips" allows for more cost-effective, efficient newborn hearing screening with the use of molecular techniques (p. 149 3rd column).

(C) The 37 CFR 1.132 asserts that Table 1 reveals that pediatric patients with SNHL unexpectedly revealed mutations in these 5 genes (point 8). The 37 CFR 1.132 asserts that Dr. John H. Greinwald was aware of no teaching or suggesting in the literature that CDH23, MYO7A, OTOF, SLC26A4, and USH2A are key components in SNHL (point 10).

This argument has been fully reviewed but has not been found persuasive.

The claims are drawn to an array comprising these 5 genes and functional limitations are not considered for patentability. In the instant case all of these genes were previously associated with hearing loss as taught by Morton et al. Choo et al. further teaches reasons for placing genes associated with hearing loss on a microarray.

(D) The 37 CFR 1.132 asserts that one of skill in the art would not know based on a list of genes to pick the 5 specific genetic sequences claimed (point 11).

This argument has been fully reviewed but has not been found persuasive.

The claims are drawn to an array comprising sequences from the 5 specific genes. The claims are not limited to an array consisting only of sequences from the 5 specific genes. Therefore the array can comprise any number of other genes and

therefore could comprise a much larger list than the one contemplated by the instant application.

Conclusion

9. No Claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to KATHERINE SALMON whose telephone number is (571)272-3316. The examiner can normally be reached on Monday-Friday 8AM-430PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Katherine Salmon/
Examiner, Art Unit 1634

/Ram R. Shukla/
Supervisory Patent Examiner, Art Unit 1634